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# EFFICACY OF NUTRITIONAL ERGOGENIC AIDS IN HOT ENVIRONMENTS

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ABSTRACT: Many athletes seeking a competitive edge rely on nutritional ergogenic aids to improve performance. Carbohydrate (CHO) and caffeine (CAF) supplementation appear efficacious at enhancing endurance exercise performance when studied under ideal circumstances, but the unique challenges imposed by environmental stressors such as heat may minimize or negate these effects. Similar to findings in temperate or cool environments, CHO intake during endurance exercise in hot environments produces a consistent performance benefit. But in contrast to the benefits observed in moderate environments, CAF affords no apparent performance advantage in the heat. These findings raise interesting questions about nutritional ergogenic mechanisms of action and offer direction for future research.

KEY WORDS: Caffeine, Carbohydrate, Endurance Performance, Heat

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## INTRODUCTION

The aerobic energy system used in endurance exercise requires nutritional support for optimal athletic performance. It has been well documented that athletes require more food energy, especially from carbohydrates (CHO), to fuel high training volumes (American College of Sports Medicine, 2009). Beyond a calorically adequate diet rich in CHO, endurance athletes may also rely upon nutritional supplements in an effort to optimize nutrition and potentially gain a competitive edge. While the market abounds with myriad ergogenic nutritional sports aids, few have consistently demonstrated performance benefits for endurance exercise. CHO and caffeine (CAF) have both been widely studied and appear to reliably enhance endurance performance under ordinary sporting circumstances (Hawley et

al., 1997; Coyle, 2004; Doherty and Smith, 2004; Hargreaves et al., 2004).

Most nutritional ergogenic aids are studied under near-ideal conditions, but exposure to environmental stressors such as heat can result in profound decrements in aerobic performance (Galloway and Maughan, 1997; Ely et al., 2007; Ely et al., 2010). Relatively few studies have explicitly addressed whether CHO or CAF can abate or surmount the performance challenges imposed by the heat, but athletic competitions regularly occur in warm weather venues. The purpose of this paper is to succinctly review the limitations to endurance exercise imposed by hot environments, explore potential mechanisms by which CHO and CAF might offset performance decrements, and examine the performance evidence.

# PERFORMANCE LIMITING FACTORS IN HOT ENVIRONMENTS

A large maximal oxygen uptake (VO<sub>2max</sub>) is a prerequisite for success in sports where aerobic endurance is contested. Although high fitness and positive heat acclimation status will dampen the negative effects of heat stress (Pandolf, 1979), acute exposure to heat stress reduces VO<sub>2mm</sub> as a consequence of displaced peripheral blood flow and a reduction in maximal cardiac output (Rowell et al., 1969; Nybo et al., 2001; Gonzalez-Alonso and Calbet, 2003). Sustainable, submaximal exercise intensities are therefore reduced since the same workload requires a larger fractional utilization of oxygen (Arngrimsson et al., 2003). The substantial body heat storage that frequently occurs with exercise in the heat can also impair motor-neural function (Nybo and Nielsen, 2001a) and cerebral blood flow (Nybo and Nielsen, 2001b), and accelerate CHO substrate depletion (Febbraio, 2000; Jentjens et al., 2002) at a time when oxidation rates of ingested CHO are simultaneously reduced (Jentjens et al., 2002). Sweat losses can be very high during exercise-heat stress as evaporative sweating is the principal means of heat loss when air temperatures are high (> 35°C). Because sweat losses frequently outmatch fluid intake, dehydration ensues and can accentuate performance-limiting factors (Gonzalez-Alonso et al., 1997; Gonzalez-Alonso et al., 2000; Nybo et al., 2001; Cheuvront et al., 2003). The same work task in the heat is also often perceived as more difficult than in temperate conditions (Nybo and Nielsen, 2001c).

Although performance-limiting factors occur in concert, rather than in isolation, one or more factors may predominate. For example, the duration of exercise is inversely proportional to its intensity, so the potential for heat to accelerate substrate depletion will become more important as exercise duration increases. The rate of heat storage, sweating rate/efficiency, and overall balance between heat gain and heat loss will also depend on the exercise intensity x environment (air temperature x humidity) interaction. It is clear, however, that even when controlling for substrate depletion, excessive heat storage, and hydration, performance is reduced by 15-20% for exercise of only 15-min duration when air temperature is increased from 20-40°C (Ely et al., 2010). The magnitude of the heat stress effect can be calibrated against a similar performance decrement (for the same exercise duration) observed when ascending from sea level to 3,000m altitude (Mazzeo and Fulco, 2006). It therefore appears that environmental heat stress impairs aerobic exercise performance reliably, but variably, depending on circumstance.

# HOW MIGHT CHO OR CAF IMPROVE PERFORMANCE?

CHO is the most efficient fuel source (i.e., more ATP is produced per unit of oxygen consumed) during exercise and ample CHO stores are necessary for sustaining high levels of performance during endurance exercise. The human body has a limited glycogen storage capacity, and CHO intake during endurance events (i.e., 42km marathon, Ironman triathlon) is considered critical for maintaining performance. The ergogenicity of CHO supplementation for endurance exercise has been widely studied. Recommendations for athletes looking to optimize performance include a high-CHO pre-exercise snack and 30-60g/hr of CHO for events lasting longer than one hour (American College of Sports Medicine, 2009). Pre-exercise CHO loading delays fatigue (Hawley et al., 1997) and consumption of CHOelectrolyte sports beverages during activity provides fuel to muscles and delays hypoglycemia, thereby maintaining central nervous system (CNS) function (Nybo, 2003). CHO may also reduce the perception of effort (Nybo, 2003) or possibly improve motivation and central drive via putative CHO receptors in the mouth (Carter et al., 2004).

The efficacy of CAF has been demonstrated consistently across a range of intakes from 3 – 13 mg/kg, but with no apparent dose-response relationship (Doherty and Smith, 2004). Several potential ergogenic benefits of CAF have been investigated. The original mechanism believed responsible for CAF's ergogenic effects with endurance exercise centered about increased adrenergic mobilization of free fatty acids and the consequent conservation of glycogen stores. However, the fragility of this explanation is now clear and it is no longer a tenable primary hypothesis (Graham, 2001). *In vitro*, CAF induces skeletal muscle contraction without membrane depolarization by interacting with calcium channels of the sarcoplasmic reticulum.

However, the dose of caffeine required to elicit this response is beyond the range associated with toxicity in humans (Davis et al., 2003; Kalmar and Cafarelli, 2004). The present leading mechanistic explanation for CAF's performance-enhancing potential is adenosine receptor antagonism. CAF acts as a CNS stimulant by blocking adenosine binding sites (Davis et al., 2003; Kalmar and Cafarelli, 2004). During endurance exercise, this may delay fatigue by increasing dopamine binding. As 'central fatigue' could be related to hyperthermia (Nybo and Nielsen, 2001a) through a neurotransmitter phenomenon, this might afford a potential performance benefit during conditions of environmental heat stress (Watson et al., 2005). The well-established analgesic effect of CAF to reduce the perception of pain (Motl et al., 2003) and effort (Doherty and Smith, 2005) would also be advantageous.

#### EFFICACY OF CHO IN THE HEAT

CHO supplementation in the heat produces a consistent performance benefit during long-duration activities (Table 1). The effect appears most pronounced (9-24% improvement) in protocols using a fixed-intensity time to exhaustion [TTE] as a measure of performance (Carter et al. 2003; Carter et al. 2005; Nassif et al. 2008), where the provision of CHO affords an extended exercise duration. However, effects are also seen in time-trial performance measures [TT] when preceded by a fixedintensity pre-load (Davis et al. 1988a; Davis et al. 1988b; Millard-Stafford et al., 1992; Below et al. 1995; Millard-Stafford et al., 1997). When benefits of CHO are observed in the heat, the magnitude of the effect appears similar to what has been reported for CHO supplementation in temperate environments. However, the number of direct experimental comparisons between hot and cooler environments is limited (Febbraio et al., 1996).

TT's simulate the strategy and bioenergetics of genuine competitive events, thus the smaller (3-10%) improvements seen in TT's may be more applicable to standard athletic competitions (e.g., 15km or 42km running events). Millard-Stafford et al. (1992) showed a substantial improvement in the final 5km of a 40km run in warm conditions with a 7% CHO-electrolyte beverage when compared to an artificially-sweetened placebo. Nassif et al. (2008) found a similar benefit with a 60%VO TTE test when volunteers were aware that they were consuming CHO in beverage form, but found no benefit in a double-blind trial when CHO was consumed in capsule form with water. This interesting difference may be attributed to a psychological benefit of CHO consumption, or to the activation of oral and pharyngeal CHO receptors that may additionally influence fatigue (Carter et al. 2004). Other studies investigating differences in CHO beverage concentration (Davis et al., 1988a; Davis et al., 1988b; Below et al., 1995; Febbraio et al., 1996; Galloway and Maughan, 2000) or the sweetness of CHO (Carter et al., 2005) have found minimal differences, although the standard 6-8% CHO beverages (-30-60gCHO/hr) are used most often for optimal absorption. Importantly, consumption of CHO in beverage form allows diminishing fluid and electrolytes levels to

be replenished simultaneously during exercise in the heat, which additionally improves performance as compared to a concentrated CHO bolus with minimal fluid replacement (Below et al., 1995) and offers a vast improvement over exercise in the heat with no fluid or carbohydrate replacement alone (Galloway and Maughan, 2000). depletion, and dehydration to influence performance in a hot, dry environment (40°C, 25%rh), Cheuvront et al. (2009) still found no advantage of CAF over placebo during a 15-min TT preceded by a 30-min exercise pre-load at 50% of VO<sub>2max</sub>. Although CAF appears to afford a small improvement in the measurement of maximal voluntary

TABLE 1. Summary of exercise performance with CHO in the heat. \*denotes significant improvement; TTE= time to exhaustion; TT=time trial performance; CE= cycle ergometry. All TT protocols involve a submaximal preload of varying duration except Millard-Stafford et al., 1990.

	PERFORMANCE TASK	ENVIRONMENT	CHO DOSE	% BENEFIT
Davis 1988a	CE at 65% max, 3x3-min time trial (TT)	26-28°C, 67-68% rh	During exercise	3-6% faster
Davis 1988b	CE at 75% max, -30 min time trial (TT)	26-28°C, 67-68% rh	During exercise	9% faster*
Millard-Stafford 1990	Swim 1.5km, CE 40km, run 10km (TT)	30°C, 67% rh	During exercise	1% faster
Millard-Stafford 1992	Run 40km; final 5km hard (TT)	25-32°C, 62-82% rh	Before + during	10% faster*
Below 1995	CE, 50-min submax, 10-min time trial (TT)	31.2°C, 54% rh	During exercise	6% faster*
Febbraio 1996	CE at 70% max to fatigue (TTE)	33°C, 20-30% rh	Before + during	<5% longer
Millard-Stafford 1997	Run 15km; final 1.6km hard (TT)	27-28°C, 62-76% rh	Before + during	5% faster*
Carter 2003	CE at 60-73% max to fatigue (TTE)	35°C, 30% rh	Before + during	18-19% longer*
Carter 2005	CE at 60% max to fatigue (TTE)	35°C, 30% rh	Before + during	12-16% longer*
Byrne 2005	3x60-min loaded walks (TTE)	35°C, 55% rh	Before + during	9% longer
Bailey 2008	CE, submax to fatigue (TTE)	35°C, 70% rh	During exercise	9% longer*
Nassif 2008	CE 60% max to fatigue (TTE)	28°C, 79% rh	During exercise	11-24% longer*

#### EFFICACY OF CAF IN THE HEAT

The ability for CAF to improve endurance performance in a temperate environment has been well established (Doherty and Smith, 2004). However, when supplemented in hot environments, null findings prevail. Cohen et al. (1996) compared a range of CAF intakes during a half-marathon (21km, ~90 minutes) running competition at WBGT 24-28°C and found no effects. The authors speculated that the -4% dehydration incurred during completion of the competitive 21km run may have obscured or overwhelmed the potential benefits of CAF. However, similar null results were also seen in a 45km cycling TT (-90 minutes) when fluid ingestion was permitted (Ferreira et al., 2005). When controlling the potential for excessive hyperthermia, substrate contractions interspersed throughout prolonged, submaximal exercise in the heat (Del Coso et al., 2008), this has yet to translate into a demonstrable exercise performance advantage.

Table 2 summarizes the small effects of CAF (1-4%) on performance in the heat, which are substantially less than the effects reported for temperate environments (-12%) (Doherty and Smith, 2004). Heat stress per se reduces performance (Ely et al., 2010) while increasing performance variability (Tyler and Sunderland, 2008; Cheuvront et al., 2009;), thus small effects might be obscured by added measurement noise. But large inconsistencies in individual responses to CAF, apparent within the Table 2 studies, suggest a genuine non-phenomenon.

TABLE 2. Summary of exercise performance with CAF in the heat. \*denotes significant improvement vs. placebo; TT= time trial performance; CE= cycle ergometry

	PERFORMANCETASK	ENVIRONMENT	CAF DOSE	% BENEFIT
Cohen 1996	21-km running race (TT)	WBGT 24-28°C	5 mg·kg <sup>-1</sup> 9 mg·kg <sup>-1</sup>	1% faster <1% slower
Ferreira 2005	45-km cycling race (TT)	28-32°C; 71-78% rh (WBGT 24.5-27°C)	5 mg·kg <sup>-1</sup> 9 mg·kg <sup>-1</sup>	4% faster 1% faster
Del Coso 2008	CE at 63% max for 120-min with 4x4-sec power measurements (TT)	36°C 29% rh	6 mg·kg <sup>-1</sup>	3% increase in power*
Cheuvront 2009	CE, 30 min at 50% max, 15-min time trial (TT)	40°C, 25% rh	9 mg·kg⁻¹	2.5% more work

The combination of CHO and CAF may also have a synergistic metabolic effect (Yeo et al., 2005) and might improve endurance performance in the heat as a consequence (Cureton et al., 2007; Del Coso et al., 2008). Many nutrition products (energy drinks, gels or chews, even soft drinks) targeted toward endurance athletes contain both CAF (25-100mg per serving) and CHO (-25 g per serving), which may work in concert to delay fatigue (Del Coso et al., 2008), reduce sensation of effort and possibly improve performance in a warm or hot environment (Cureton et al., 2007). Further study of CAF and CHO combinations in a hot environment may be a fertile area for future research.

## CONCLUSIONS

Environmental heat stress poses a unique challenge to endurance performance and may reduce or negate the efficacy of established nutritional ergogenic aids. CHO and CAF are among the few nutritional ergogenic aids with recognized legitimacy in ordinary environments. When examined against the larger body of literature, comparably fewer studies have examined the potential efficacy of CHO or CAF in hot environments (Tables 1, 2). Although a variety of performance tests, exercise intensities, and exercise durations have been used over a range of warm to hot environments, study outcomes show a consistent significant benefit of CHO (8/12 studies) in the heat but no benefit of CAF (0/4 studies). These observations raise important questions concerning the underlying mechanism(s) of CHO and CAF ergogenicity and also support future study of the potential ergogenic interaction of CHO and CAF for enhancing endurance exercise performance in hot environments.

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# REFERENCES

American College of Sports Medicine (2009) Nutrition and athletic performance position stand. *Medicine & Science in Sports & Exercise* 41, 709-731.

Arngrimsson, S.A., Stewart, D.J., Borrani, F., Skinner, K.A. and Cureton, K.J. (2003) Relation of heart rate to percent VO<sub>2peak</sub> during submaximal exercise in the heat. *Journal of Applied Physiology* 94, 1162-1168.

Bailey, S.P., Holt, C., Pfluger, K.C., La Budde, Z., Afergan, D., Stripling, R., Miller, P.C. and Hall, E.E. (2008) Impact of prolonged exercise in the heat and carbohydrate supplementation on performance of a virtual environment task. *Military Medicine* 173, 187-192.

Below, P.R., Mora-Rodriguez, R., Gonzalez-Alonso, J. and Coyle, E.F. (1995) Fluid and carbohydrate ingestion independently

improve performance during 1 h of intense exercise. Medicine & Science in Sports & Exercise 27, 200-210.

Byrne, C., Lim, C.L., Chew, S.A. and Ming, E.T. (2005) Water versus carbohydrate-electrolyte fluid replacement during loaded marching under heat stress. *Military Medicine* 170, 715-721.

Carter, J., Jeukendrup, A.E. and Jones, D.A. (2004) The effect of carbohydrate mouth rinse on 1-h cycle time trial performance. Medicine & Science in Sports & Exercise 36, 2107-2111.

Carter, J., Jeukendrup, A.E. and Jones, D.A. (2005) The effect of sweetness on the efficacy of carbohydrate supplementation during exercise in the heat. *Canadian Journal of Applied Physiology* 30, 379-391.

Carter, J., Jeukendrup, A.E., Mundel, T. and Jones, D.A. (2003) Carbohydrate supplementation improves moderate and highintensity exercise in the heat. *Pflugers Archive* 446, 211-219

Cheuvront, S.N., Carter, R. III, and Sawka, M.N. (2003) Fluid balance and endurance exercise performance. *Current Sports Medicine Reports* 2(4), 202-208.

Cheuvront, S.N., Ely, B.R., Kenefick, R.W., Michniak-Kohn, B.B., Rood, J.C. and Sawka, M.N. (2009) No effect of nutritional adenosine receptor antagonists on exercise performance in the heat. *American Journal of Physiology-Regulatory, Integrative & Comparative Physiology* 296, R394-R401.

Cohen, B.S., Nelson, A.G., Prevost, M.C., Thompson, G.D., Marx, B.D. and Morris, G.S. (1996) Effects of caffeine ingestion on endurance racing in heat and humidity. *European Journal of Applied Physiology* 73, 358-363.

Coyle, E.F. (2004) Fluid and fuel intake during exercise. In: Maughan, R.J., Burke, L.M. and Coyle, E.F. (Eds), Food, nutrition and sports performance II (Abingdon: Routledge Publishers) pp.63-91.

Cureton, K.J., Warren, G.L., Millard-Stafford, M.L., Wingo, J.E., Trilk, J. and Buyckx, M. (2007) Caffeinated sports drink: ergogenic effects and possible mechanisms. *International Journal of Sports Nutrition & Exercise Metabolism* 17, 35-55.

Davis, J.M., Burgess, W.A., Slentz, C.A., Bartoli, W.P. and Pate, R.R. (1988a) Effects of ingesting 6% and 12% glucose/electrolyte beverage during prolonged intermittent cycling in the heat. *European Journal of Applied Physiology* 57, 563-569.

Davis, J.M., Lamb, D.R., Pate, R.R., Slentz, C.A., Burgess, W.A. and Bartoli, W.P. (1988b) Carbohydrate-electrolyte drinks: effects on endurance cycling in the heat. *American Journal of Clinical Nutrition* 48, 1023-1030.

Davis, J.M., Zhao, Z., Stock, H.S., Mehl, K.A., Buggy, J. and Hand, G.A. (2003) Central nervous system effects of caffeine and adenosine on fatigue. American Journal of Physiology-Regulatory, Integrative & Comparative Physiology 284, R399-R404.

Del Coso, J. Estevez, E. and Mora-Rodriguez, R. (2008) Caffeine effects on short-term performance during prolonged exercise in the heat. Medicine & Science in Sports & Exercise 40, 744-751.

Doherty, M. and Smith, P.M. (2005) Effects of caffeine ingestion on ratings of perceived exertion during and after exercise: a metaanalysis. Scandinavian Journal of Medicine & Science in Sports 15, 69-78.

Doherty, M. and Smith, P.M. (2004) Effects of caffeine ingestion on exercise testing: a meta-analysis. International Journal of Sports Nutrition & Exercise Metabolism 14, 626-646.

Ely, B.R., Cheuvront, S.N., Kenefick, R.W. and Sawka, M.N. (2010) Aerobic performance is degraded, despite modest hyperthermia, in hot environments. Medicine & Science in Sports & Exercise 42, 135-141.

Ely, M.R., Cheuvront, S.N., Roberts, W.O. and Montain, S.J. (2007) Impact of weather on marathon-running performance. Medicine & Science in Sports & Exercise 39, 487-493.

Febbraio, M.A. (2000) Does muscle function and metabolism affect exercise performance in the heat? Exercise and Sport Sciences Reviews 28, 171-176.

Febbraio, M.A., Murton, P., Selig, S.E., Clark, S.A., Lambert, D.L., Angus, D.J. and Carey, M.F. (1996) Effect of CHO ingestion on exercise metabolism and performance in different ambient temperatures. Medicine & Science in Sports & Exercise 28, 1380-1387.

Ferreira, G.M., Guerra, G.C. and Guerra, R.O. (2005) Effect of caffeine in the performance of cyclists under high thermal risk. [article in Portuguese] Acta Cirurgica Brasileira 20, 196-203.

Galloway, S.D. and Maughan, R.J. (1997) Effects of ambient temperature on the capacity to perform prolonged cycle exercise in man. Medicine & Science in Sports & Exercise 29, 1240-1249.

Galloway, S.D. and Maughan, R.J. (2000) The effects of substrate and fluid provision on thermoregulatory and metabolic responses to prolonged exercise in a hot environment. Journal of Sports Sciences 18, 339-351.

Gonzalez-Alonso, J. and Calbet, J.A. (2003) Reductions in systemic and skeletal muscle blood flow and oxygen delivery limit maximal aerobic capacity in humans. Circulation 170, 824-830.

Gonzalez-Alonso, J., Mora-Rodriguez, R., Below, P.R. and Coyle,

E.F. (1997) Dehydration markedly impairs cardiovascular function in hyperthermic endurance athletes during exercise. Journal of Applied Physiology 82, 1229-1236.

Gonzalez-Alonso, J., Mora-Rodriguez, R. and Coyle, E.F. (2000) Stroke volume during exercise: interaction of environment and hydration. American Journal of Physiology- Heart and Circulatory Physiology 278, H321-H330.

Graham, T.E. (2001) Caffeine and exercise. Metabolism, endurance and performance. Sports Medicine 31, 785-807.

Hargreaves, M., Hawley, J.A. and Jeukendrup, A.E. (2004) Pre-exercise carbohydrate and fat ingestion: effects on metabolism and performance. In: Maughan, R.J., Burke, L.M. and Coyle, E.F. (Eds), Food, nutrition and sports performance II (Abingdon: Routledge Publishers) pp. 50-

Hawley, J.A., Schabort, E.J., Noakes, T.D. and Dennis, S.C. (1997) Carbohydrate-loading and exercise performance. An update. Sports Medicine 24, 73-81.

Jentjens, R.L., Wagenmakers, A.J. and Jeukendrup, A.E. (2002) Heat stress increases muscle glycogen use but reduces the oxidation of ingested carbohydrates during exercise. Journal of Applied Physiology 92, 1562-1572.

Kalmar, J.M. and Cafarelli, E. (2004) Caffeine: a valuable tool to study central fatigue in humans? Exercise and Sport Sciences Reviews 32, 143-147.

Mazzeo, R.S. and Fulco, C.S. (2006) Physiological systems and their responses to conditions of hypoxia. In: Tipton, C.M. (Ed), ACSM's Advanced Exercise Physiology (Baltimore: Lipincott Williams & Wilkins), pp.564-580.

Millard-Stafford, M.L., Rosskopf, L.B., Snow, T.K. and Hinson, B.T. (1997) Water versus carbohydrate-electrolyte ingestion before and during a 15-Km run in the heat. International Journal of Sports Nutrition 7, 26-38.

Millard-Stafford, M.L., Sparling, P.B., Rosskopf, L.B. and Dicarlo, L.J. (1992) Carbohydrate-electrolyte replacement improves distance running performance in the heat. Medicine & Science in Sports & Exercise 24, 934-940.

Millard-Stafford, M.L., Sparling, P.B., Rosskopf, L.B., Hinson, B.T. and Dicarlo, L.J. (1990) Carbohydrate-electrolyte replacement during a simulated triathlon in the heat. Medicine & Science in Sports & Exercise 22, 621-628.

Motl, R.W., O'Connor, P.J. and Dishman, R.K. (2003) Effect of caffeine on perceptions of leg muscle pain during moderate intensity cycling exercise. Journal of Pain 4, 316-321.

Nassif, C., Ferreira, A.P., Gomes, A.R., Silva, L.D., Garcia, E.S. and Marino, F.E. (2008) Double blind carbohydrate ingestion does not improve exercise duration in warm humid conditions. *Journal of Science and Medicine in Sport* 11, 72-79.

Nybo, L. (2003) CNS fatigue and prolonged exercise: effect of glucose supplementation. *Medicine & Science in Sports & Exercise* 35, 589-594.

Nybo, L., Jensen, T., Nielsen, B. and Gonzalez-Alonso, J. (2001) Effects of marked hyperthermia with and without dehydration on VO<sub>2</sub> kinetics during intense exercise. *Journal of Applied Physiology* **90**, 1057-1064.

Nybo, L. and Nielsen, B. (2001a) Hyperthermia and central fatigue during prolonged exercise in humans. *Journal of Applied Physiology* 91, 1055-1060.

Nybo, L. and Nielsen, B. (2001b) Middle cerebral artery blood velocity is reduced with hyperthermia during prolonged exercise in humans. *Journal of Physiology* 534, 279-286.

Nybo, L. and Nielsen, B. (2001c) Perceived exertion is associated with altered brain activity during exercise with progressive hyperthermia. *Journal of Applied Physiology* 91, 2017-2023.

Pandolf, K.B. (1979) Effects of physical training and cardiorespiratory fitness on exercise-heat tolerance: recent observations. *Medicine & Science in Sports & Exercise* 11, 60-65.

Rowell, L.B., Murray, J.A., Brengelmann, G.L. and Kraning, K.K. (1969) Human cardiovascular adjustments to rapid changes in skin temperature during exercise. *Circulation Research* 24, 711-724.

Tyler, C. and Sunderland, C. (2008) The effect of ambient temperature on the reliability of a preloaded treadmill time-trial. *International Journal of Sports Medicine* 29, 812-816.

Watson, P., Hasegawa, H., Roelands, B., Piacentini, M.F., Looverie, R. and Meeusen, R. (2005) Acute dopamine/noradrenaline reuptake inhibition enhances human exercise performance in warm, but not temperate conditions. *Journal of Physiology* 565, 873-883.

Yeo, S.E., Jentjens, R.I., Wallis, G.A. and Jeukendrup, A.E. (2005) Caffeine increases exogenous carbohydrate oxidation during exercise. *Journal of Applied Physiology* 99, 844-850.